SERUM ANTIOXIDANTS VITAMINS C AND E STATUS IN CANCER PATIENTS IN ZARIA

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ABSTRACT

Background; There are several studies showing disturbances in antioxidant defence systems in the pathogenesis of cancer. Studies in cell cultures show that vitamins C and E, selenium and some phytochemicals selectively induce apoptosis in cancer cells while sparing normal cells. Numerous studies have shown a depletion of antioxidants and increased amount of ROS in patients with malignancies but no such study have been carried out on cancer patients in Zaria.

Aim; To evaluate the status of antioxidants vitamins C and E in the serum of cancer patients and aged sex matched controls in Zaria.

Methodology; One hundred and seventeen cancer patients who were histologically or cytologically confirmed and an equal number of apparently healthy aged and sex-matched controls were recruited by simple random sampling. Blood samples were analysed for serum antioxidant vitamins C and E using direct colorimetric methods.

Results; The average age of the participants were 57years with a male to female ratio of 1:1.1. The serum concentrations of both vitamin C and E were significantly lower compared to the controls with no significant difference in the mean values of vitamin C and E in both males and females.

Conclusion; Cancer is commoner among the middle age group with female preponderance. The serum levels of antioxidant vitamins C and E were lower in cancer compared to controls**.**

Key words; Antioxidant, Cancer, Vitamin C, Vitamin E

INTRODUCTION

Cancer is defined as the malignant form of uncontrolled growth of cells and tissues. *(*Sriharikrishnaa, *et al*., 2023). It is a dreaded non-communicable disease in developing countries where it is invariably fatal, due to lack of adequate preventive and curative services. This is unlike in developed countries where policies, strategies and programs for cancer prevention and management are available (Silbermann, 2016). Endogenous antioxidants that neutralize reactive oxygen species act as cancer scavengers in humans (Ahmed & Mohammed, 2020). Human observational studies have indicated that oxidative stress increases with clinical progression of cancer, causing more consumption of antioxidants, while antioxidant rich diets reduce the risk of certain cancers (Milkovic, *et al.,* 2014). Studies in cell cultures showed that vitamins C and E, selenium and some phytochemicals selectively induce apoptosis in cancer cells while sparing normal cells (Borek, 2008).

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Vitamin E is the main lipid-soluble chain-breaking antioxidant present in membranes and plasma (Borek, 2008).Vitamin C is also a major and extremely versatile antioxidant in plasma (Borek, 2008). They are capable of preventing initiation of lipid peroxidation, while other water-soluble antioxidants such as betacarotene, bilirubin, uric acid and thiol-compounds (mainly plasma proteins) are only effective in decreasing the rate of lipid peroxidation. Numerous studies have shown a depletion of antioxidants and an increased amount of reactive oxygen species in patients with malignancies (Vostrikova, *et al* 2020). No similar study has been carried out on the level of lipid peroxidation and antioxidants levels in cancer patients in our environment. The present study is therefore undertaken to evaluate the status of antioxidant vitamins C and E in the serum of radiologically diagnosed and histologically or cytologically confirmed cancer patients and controls in Zaria.

MATERIALS AND METHODS

This was a descriptive cross-sectional study conducted at the Oncology Clinic of Ahmadu Bello University Teaching Hospital (ABUTH) Shika, Zaria over a period of thirteen months. A total number of 117 radiologically diagnosed and histologically or cytologically confirmed diagnosis of cancer with equal number of age-sex matched controls were recruited for this study. The chemicals and reagent kits used for the determination of serum antioxidant vitamin C and E levels were procured from Randox Chemicals Limited and M&B limited (England). Blood samples were analysed for serum vitamins C and E using colorimetric methods. Ascorbic acid was oxidized by ascorbate oxidase resulting in the production of H_2O_2 which reacted with a specific dye to form a pink colored product (Jagota & Dani, 1982). The color intensity at 570nm was directly proportional to the ascorbic acid concentration in the sample (Jagota & Dani, 1982). Tocopherol (vitamin E) produced a colored reaction with batophenanthroline, $FeCl_3$ and H_3PO_4(30). The intensity of the color formed, measured at 539nm was directly proportional to the concentration of vitamin E in the sample (Elden *et al*., 2016). Adequate quality control was done by analysing the samples in batches together with quality control sera both intra- batch and inter- batch for specific analytes.

The data obtained was analyzed using SPSS 25.0. Continuous variable was compared using the two tailed student's t-test. A p-value ($p \leq 0.05$) was considered statistically significant.

RESULTS

The mean age of the study participants was 57.43 ± 11.2 years, while that of the controls was 56.14 ± 03.2 years (p= 0.991). The patients comprised of 57 (48%) males and 60 (52%) females while the controls were 55 (47%) males and 62 (53%) females. The male to female ratio was 1:1.1 in both the patients and controls respectively. The mean age for the male patients was 62.81 ± 11.0 years and 61.80 ± 11.1 years for the controls, while the female was 52.30 ± 08.7 years and 53.70 ± 07.8 years for the patients and controls respectively. There was no significant difference in the mean gender ages between patients and controls, p-values was 0.630 and 0.450 for both males and females respectively as shown in table 1.

Table 1: Gender distribution of study population

	Patients		Controls			
Sex	n (%)	Mean ±SD	n (%)	Mean ±SD	t	p-value
Male	57(48)	62.81 ±11.0	55(47)	61.80 ±11.1	0.482	0.630
Female	60(52)	52.30 ± 08.7	62(53)	53.70 ± 07.8		0.450
Total	117(100)	57.43±11.2	117(100)	56.14 ± 03.2		0.991
M:F	1:1		1:1			

n=total number of individuals, SD=standard deviation, t = Test Statistic, $^{\alpha}$ Independent t-test, p=Pearson's coefficient of variation.

Table 2 showed Serum levels of vitamin C and E of cancer patients were significantly lower compared to the controls. Median (IQR) values of vitamin C were 16.55 (10.7) µmol/l and 46.89 (12.1) µmol/l for patients and controls respectively. Median (IQR) values of vitamin E were 0.19 (0.2) µmol/l and 2.99 (0.5) µmol/l for patients and controls respectively (p<0.0001).

Table 2: Serum levels of vitamin C and E among the study population

	Patients n = 117	Controls n = 117	
Analytes	Median (IQR)	Median (IQR)	p-value
Vitamin C (µmol/l)	16.55 (10.7)	46.89 (12.1)	<0.0001
Vitamin E (µmol/l)	0.19 (0.2)	2.99 (0.5)	<0.0001

n=total number of individuals, p=Pearson's coefficient of variation, IQR=Inter quatile range

Table 3 showed no significant difference in the mean values of vitamin C and E in both males and females. Median (IQR) value of vitamin C was 16.32 (10.4) µmol/l in males and 16.84 (11.0) µmol/l in females respectively (p=0.840). The Median (IQR) value of vitamin E was 0.35 (1.1) µmol/l in males and 0.10 (1.2) µmol/l in females. (p=0.905).

Table 3: Serum vitamin C and E in patients according to gender.

	Participants		
	Male	Female	
Analyte	Median (IQR)*	Median (IQR)*	p-value
Vitamin C (µmol/l)	16.32 (10.4)	16.84 (11.0)	0.840
Vitamin E (µmol/l)	0.35 (1.1)	0.10 (1.2)	0.905

n=total number of individuals, p=Pearson's coefficient of variation, IQR=Inter quatile range

DISCUSSION

The mean age of the patients in this study is similar to previous studies in Lagos (Omolara, 2011) and Ibadan (Akinloye *et al., 2009*) Nigeria where the mean ages of the cancer patients were also found to be 50years. The lower percentage of cancer seen above 50 years of age in some African studies compared to the Caucasian, may be due to the lower life expectancy and or early exposure to risk factors in Africans. These similarities may be explained because cancer is essentially a disease of the elderly, though it may occur at any age. It has been reported that more than 95% of cancers occur in persons older than 50 years of age in most regions of the world (Hamdi *et al.*, 2021). The increased incidence of cancer with advancing age may be partly due to the increasing level of free radical reactions with age and largely reflects cell DNA damage accumulating over time. Damage can result from biological processes or from exposure to risk factors.

There is also a diminishing ability of the immune system to eliminate altered cells because of immune tolerance, thus the effectiveness of cancer surveillance by immune cells is reduced with advancing age (Hamdi *et al.*, 2021). The predominance of females with cancer in this study may be also due to curiosity of the females about their health status than male counterpart which will eventually lead to more attendance in the clinic, or due to the various awareness and screening programs (e.g breast and cervical cancer screening) targeted at females. In the present study, the serum concentrations of vitamin C and E in cancer patients were low compared to controls which was similarly reported by (Abiri & Vafa, 2021). This also corroborated with other studies which showed a depletion of antioxidants in malignancies. This was similarly reported by another study in Ibadan (Akinloye *et al.*, 2009). In this study, cancer patients were found to have a significantly low serum vitamin C and E levels. This also collaborate with other studies which showed a depletion of antioxidants and increased amount of ROS in malignancies (Abiri & Vafa, 2021). Free radical production occurs as a consequence of normal endogenous reactions and plays an important role in physiological cell function (Lushchak, 2014). It is important to note that the ingestion of exogenous substances and environmental factors can also promote free radical formation, thereby leading to the depletion of cellular antioxidants (Martemucci *et al.*, 2022). Reactive oxygen species (ROS) have physiological functions, including activation and modulation of signal transduction pathways alteration of activities of redox-sensitive transcription factors and regulation of mitochondrial enzyme activities (Lennicke & Cochemé, 2021). To protect against toxic effects of ROS and to modulate physiological effects of ROS, the cell has developed an intricately regulated and a very complex antioxidant defense system (Sachdev *et al.*, 2021). It is composed of small molecular weight antioxidant compounds (vitamins E, C, A, uric acid), primary (Super Oxide Dismutase, catalase, glutathione peroxidase) and secondary antioxidant enzymes (glutathione reductase and glucose 6-phosphate dehydrogenase), and the glutathione, glutaredoxin and thioredoxin systems (Aslani & Ghobadi, 2016). In the present study, the serum levels of the antioxidant vitamins C and E decreased significantly in participants when compared to normal. This observation is consistent with most in vivo and in vitro studies which demonstrated that the levels of antioxidants are lowered in cancer (Fuchs-Tarlovsky, 2013). The findings in biochemical studies have showed that antioxidant vitamin C and E are lowered in most types of primary cancers and cancer cell lines. Studies on antioxidant vitamin C and E levels in human oral and renal cancers (Litecká *et al.*, 2020) confirmed the reduced levels of this vitamins in various cancers. Furthermore, immunoperoxidase studies demonstrated low levels of antioxidant vitamins in primary cancers, although small groups of cancer cells, often on the invading edge of the cancer, did occasionally showed elevated levels.

The mean values of vitamin C and E were similar in both the male and female participants. This is contrary to the report of another study which found gender disparities in the concentrations of antioxidants in favour of females (Kander *et al.*, 2017) It was found in that study that males have lower concentrations of antioxidants compared to females because oxidative damage to mitochondrial DNA in males is 4-fold higher than that in females. This was said to be due to higher expression and activities of antioxidants in females, which behave as double transgenics over-expressing superoxide dismutase and glutathione peroxidase, conferring protection against free-radical-mediated damage in aging. Moreover, small ribosomal RNA expression, which decreases significantly with aging, is four times higher in mitochondria from females than in those from males of the same chronological age.

These facts were said to provide molecular evidence to explain the different life span in males and females (Violi *et al.,* 2017). The reason for the difference in the results of our study from that in the literature may be due to to the larger number of participants in the previous study. Differences in dietary and nutritional intake between our population and that in the literature may also be a contributory factor.

CONCLUSION

It was found that cancer is commoner among the middle age group with female preponderance. The serum levels of antioxidant vitamins C and E were lower in cancer compared to controls.

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